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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/015,394	12/11/2001	Kevin P. Baker	39780-2830P1C41	9887

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/015,394	BAKER ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/10/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 10 January 2005 has been entered in full. Claims 1-27 and 33 are cancelled and claim 28 is amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 28-32 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 2-3 of the previous Office Action (21 October 2004) are *withdrawn* in view of the amended specification and title (10 January 2005).

2. The rejections to claims 28-33 under 35 U.S.C. 112, second paragraph, as set forth at pg 8 of the previous Office Action (21 October 2004) are *withdrawn* in view of the cancelled claim 33 (10 January 2005).

3. The rejections to claims 28-33 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph as set forth at pg 3-8 of the previous Office Action (21 October 2004) are *withdrawn in part* in view of cancelled claim 33. Please see section on 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, below.

4. The supplemental information disclosure statement filed on 10 January 2005 has been considered.

Claim Rejections - 35 USC § 101 and 35 USC § 112

5. Claims 28 and 31 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claims read on a product of nature in that the

claimed antibody is not "isolated". For example, the claims encompass polyclonal sera that has not been removed from the human or animal. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty,* 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified". See MPEP 2105. The basis for this rejection is set forth for claims 28, 31, and 33 at pg 3-4 of the previous Office Action (21 October 2004).

Applicant's arguments (10 January 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that claim 28 has been amended to recite "an isolated antibody". Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, claim 28 has not yet been amended to recite an "isolated antibody". Therefore, claims 28 and 31 still read on a product of nature.

6. Claims 28-32 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth for claims 28-33 at pg 3-5 of the previous Office Action (21 October 2004).

Claims 28-32 are directed to an antibody that binds to the polypeptide shown in Figure 220 (SEQ ID NO: 376). The claims also recite that the antibody is monoclonal or humanized. The claims recite that the antibody is an antibody fragment or that the antibody is labeled.

Applicant's arguments (10 January 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the adipocyte glucose/FFA uptake assay (Example 149) is relied upon for support of patentable utility. Applicant explains that the glucose/FFA assay is designed to determine whether a polypeptide is capable of modulating (either positively or negatively), the uptake of glucose or free fatty acids in adipocyte cells. Applicant cites Tafuri et al. (Endocrinology 137(11) : 4706-4712, 1996), Sandouk et al. (endocrinology 133(1): 352-359, 1993), Goldwaser et al. (J Biol Chem 274(37): 26617-26624, 1999), Mueller et al. (Endocrinology 139(2) : 551-558, 1998), and Mueller et al. (Obesity Research 8(7): 530-539, 2000) to support the assertion that increasing glucose uptake by adipocyte cells is a hallmark of a number of therapeutically effective agents. Applicant argues that one of skill in the art would have reasonably accepted that various compounds, such as PRO1760, that are capable of modulating glucose uptake, have a substantial, practical, real-life utility. Applicant contends that a variety of real-life utilities, such as treatments for glucose uptake related diseases, including obesity and diabetes, are envisioned for PRO1760 and its antibody based on the glucose/FFA uptake assay results disclosed therein. It is noted that Applicant reviews the legal standard for utility at pg 7-8 of the Response.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification of the instant application teaches that PRO1760 is positive as *inhibitor* of glucose and FFA uptake by adipocytes (pg 512, lines 9-10). Applicant's agent even reiterates this finding by stating at pg 9 of the Response, "As PRO1760 resulted in less then 0.5 the uptake of insulin control, PRO1760 tested positive as an inhibitor of glucose/FFA uptake in adipocyte

cells". However, each of the 5 references cited by Applicant teach that the agents utilized in the assays *enhance* glucose uptake by adipocyte cells, not inhibit glucose uptake as asserted by the instant specification. As discussed in the previous Office Action of 21 October 2004, disorders, such as obesity, diabetes, and hyper- or hypo-insulinemia have reduced glucose entering adipocyte cells. For example, Khan et al. (Diabetologia 45: 1475-1483, 2002; especially pg 1475, 1st full paragraph) teach that "type II (non-insulin-dependent) diabetes mellitus is a clinical disorder of sugar and fat metabolism caused by an inability of insulin to promote sufficient glucose uptake into adipocyte tissue and striated muscle and to prevent glucose output from the liver". Therefore, as emphasized by Tafuri et al., Sandouk et al., Goldwaser et al., Mueller et al. 1998, and Mueller et al. 2000, one skilled in the art would want to enhance glucose uptake into adipocyte cells. However, it is noted again that Applicant asserts the PRO1760 polypeptide inhibits glucose uptake in adipocyte cells. If one skilled in the art were to administer the PRO1760 polypeptide of the instant application to a patient with obesity, diabetes, and hyper- or hypo-insulinemia, the PRO1760 polypeptide would exacerbate the condition. Given the paucity of information, the data do not support the implicit conclusion of the specification that PRO1760 would be useful for the therapeutic treatment of disorders where the inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia. The proposed use of the claimed antibodies that bind PRO1760 polypeptides are simply starting points for further research and investigation into potential practical uses of the polypeptides.

Furthermore, Tafuri et al., Sandouk et al., Goldwaser et al., Mueller et al. 1998, and Mueller et al. 2000 teach different methodologies for the measurement of glucose uptake in

adipocyte cells as compared to the glucose assay of the instant specification. For instance, the instant specification teaches that "in a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and PFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control" (pg 512, lines 1-4). However, Sandouk et al. teach that 3T3-F442A cell monolayers were rinsed with PBS and incubated with assay medium for 15 min. Then, 0.5 μCi D-[U-^{14}C]glucose was added for 15 min. After this incubation, the medium was aspirated, cells were rinsed, solubilized, neutralized, and counted for radioactivity (pg 353, col 1, first full paragraph). Mueller et al. 2000 disclose that aliquots of adipocytes are incubated with different concentrations of either metformin or vanadium at 24, 48, 72, and 96 hours with or without insulin (pg 532, the bottom of col 1 through col 2). Additionally, the papers cited by Applicant report resulting numbers for the various samples of the glucose uptake assays. None of the references utilize the stimulatory and inhibitory scale disclosed in the specification (pg 512, lines 4-6). The instant specification does not report any specific cell numbers or statistical differences and there is no indication in the specification as to statistically how much the PRO1760 inhibited glucose uptake as compared to control.

In conclusion, the PRO1760 polynucleotide, polypeptide, and antibody of the instant application (SEQ ID NOs: 375 and 376, respectively) are not supported by either a credible, specific and substantial ("real-world") asserted utility or a well-established utility. The polynucleotide, polypeptide, and antibody do not have a substantial utility because basic research

is required to study the properties and activity of the polynucleotide that encodes the polypeptide of SEQ ID NO: 376. Until some actual and specific significance can be attributed to the protein identified in the specification as PRO1760, the instant invention is incomplete. In the absence of knowledge of the biological significance of this protein, there is no immediately obvious patentable use for it. If the specification discloses nothing specific and substantial about the PRO1760 polypeptide, therefore both the polypeptide and its antibodies have no patentable utilities. Since the instant specification does not disclose a "real world" use for PRO1760 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

7. Claims 28-32 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth for claims 28-33 at pg 5-8 of the previous Office Action (21 October 2004).

Applicant's arguments (10 January 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant states that a credible, substantial, and asserted utility has been disclosed above for the polypeptide PRO1760. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, since Applicant has not provided evidence to demonstrate that the PRO1760 polypeptide has a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention. It is noted that

the instant specification is required to teach one skilled in the art how to make and use the PRO1760 polypeptide and antibody.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
04 April 2005

ELIZABETH KEMMERER
PRIMARY EXAMINER